



Armed Forces College of Medicine

AFCM



Triacylglycerol Metabolism

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INTENDED LEARNING OBJECTIVES (ILOs)



➤ **By the end of this lecture, You will be able to:**

1. Illustrate sources of  cerol phosphate.
2. Mention steps of FA activation and lipogenesis.
3. Describe steps of lipolysis and its regulation.

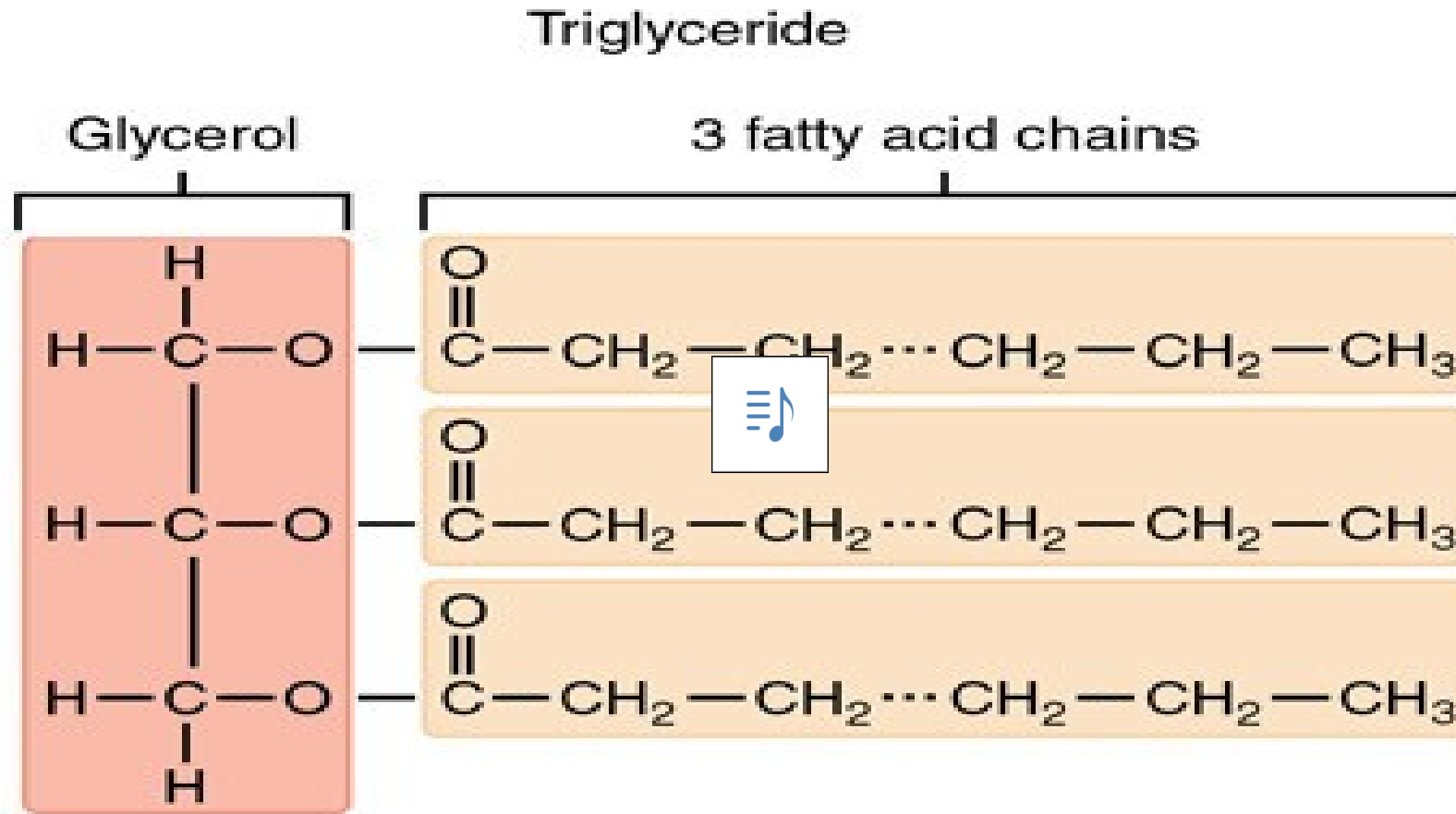
Case scenario



An **obese** 45 year old male
consulted a dietitian  for
weight loss. He advised him
to **decrease CHO** in his diet
and gave him a dietary plan
to follow.



TAG (Triacylglycerol)



<https://alevelbiology.co.uk/notes/simple-lipids-fats-oils-waxes/>

TAG (Triacylglycerol)



Storage of TAG

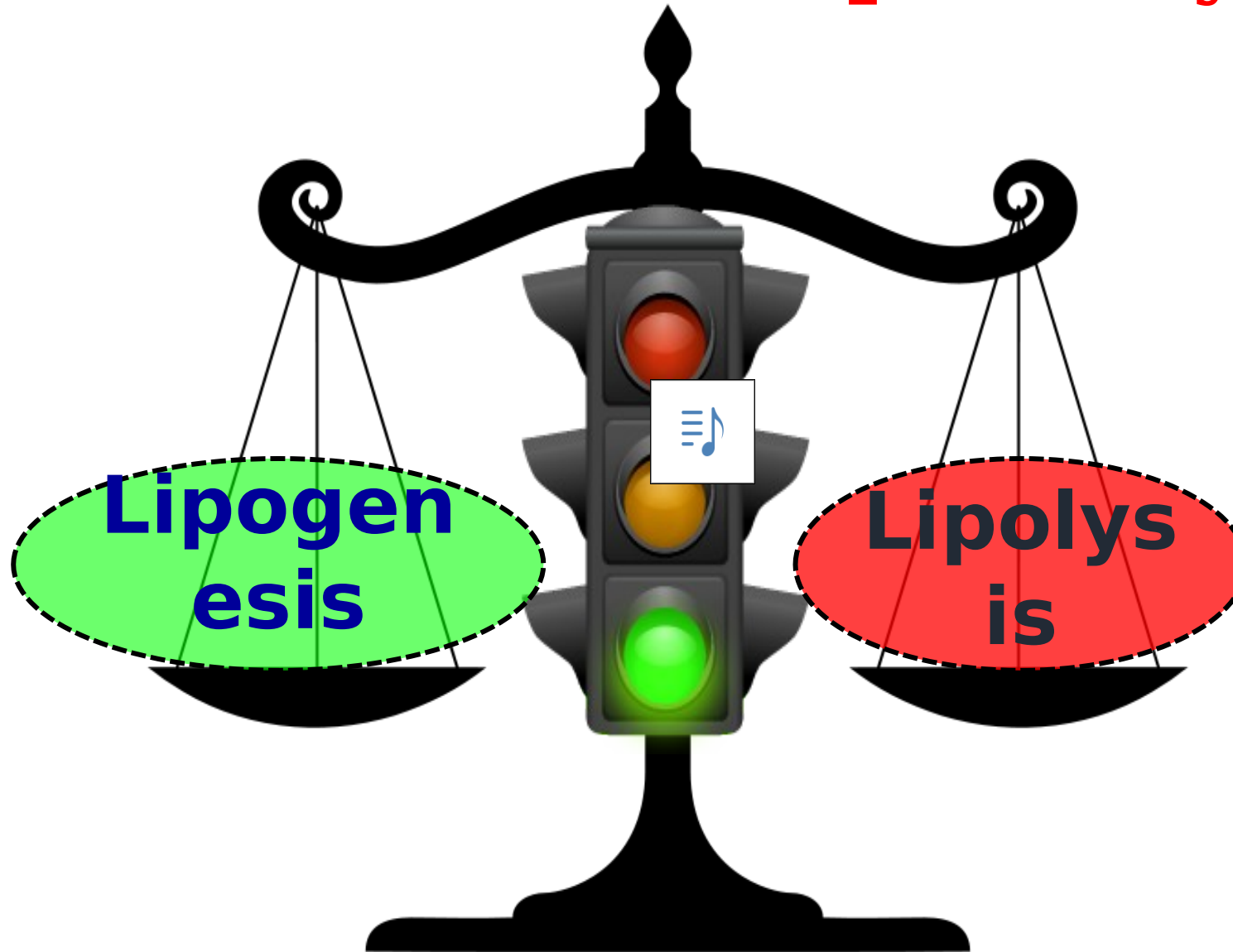
- TAG form oily droplets in cytoplasm of adipocytes (fat Cells).



- TAG lipid droplets are the major **energy reserve** of the body during **fasting and starvation.**



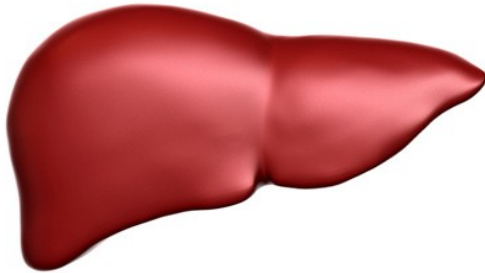
There are 2 metabolic pathways of TAG



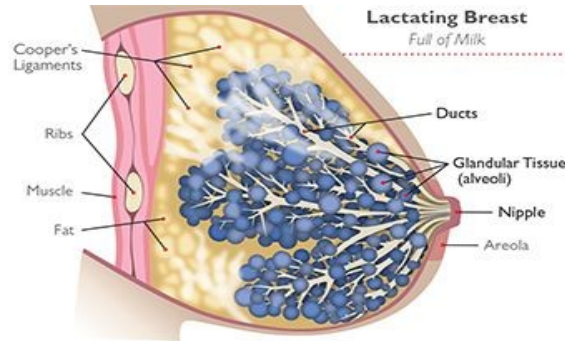
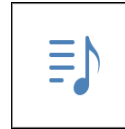
Synthesis Of TAG (lipogenesis)



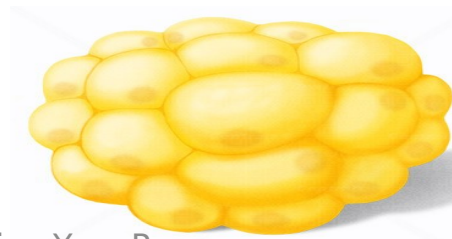
Site of TAG Syn



Liver
(primary site of TAG
synthesis)



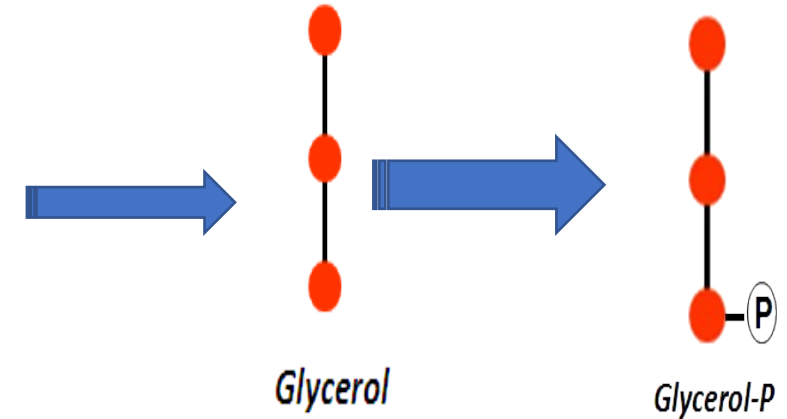
Lactating mammary gland



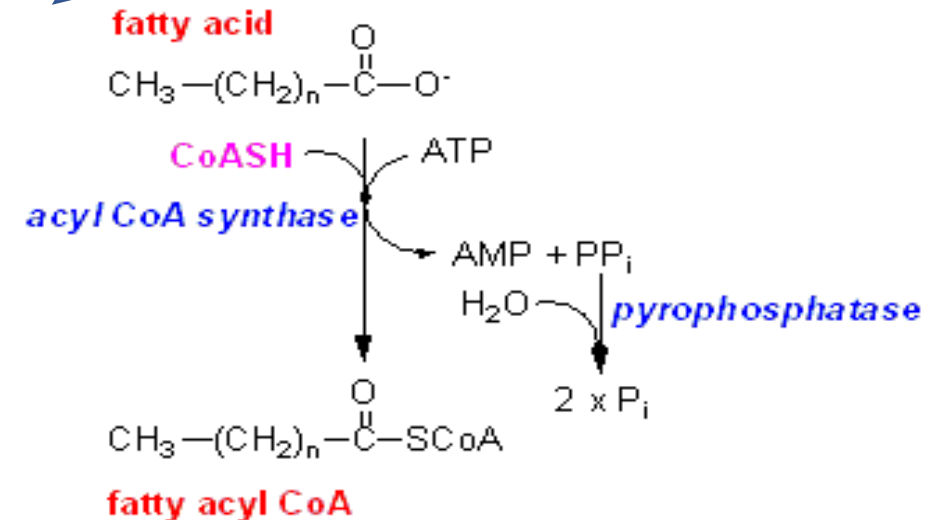
Adipose tissue

Steps of TAG Synthesis

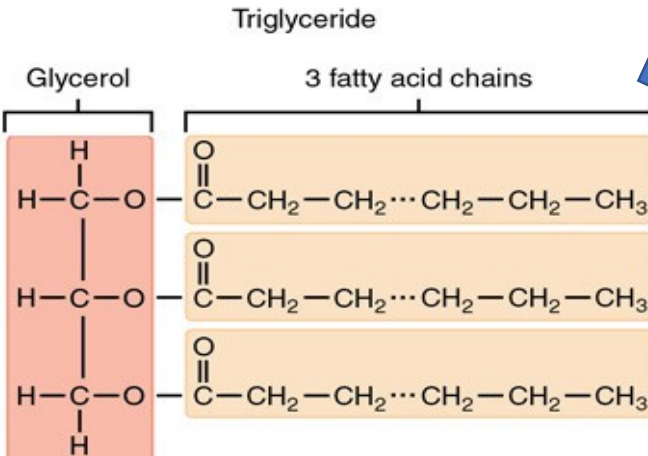
1. Activation of Glycerol → Glycerol-3-Phosphate



2. Activation of the fatty acids Fatty Acyl CoA



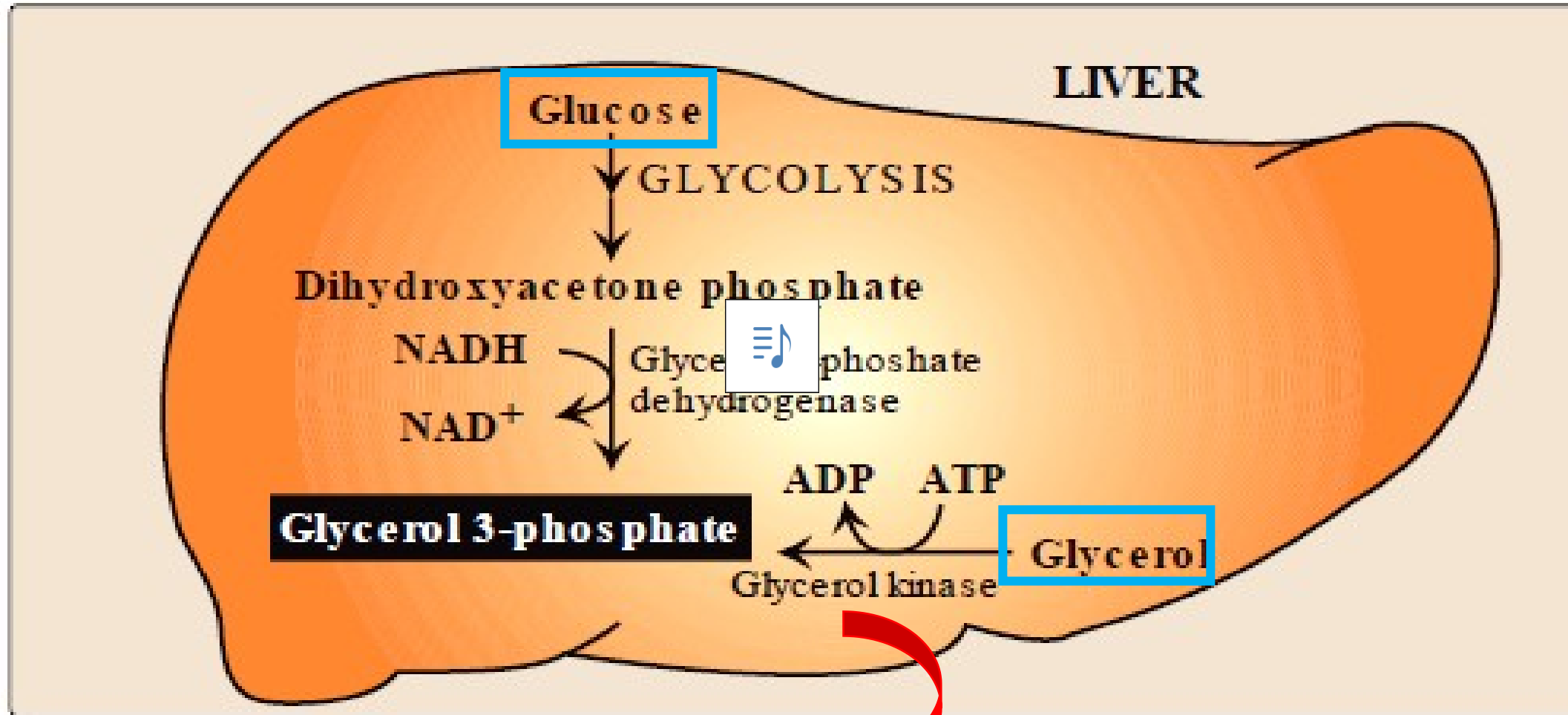
3. Esterification



Step 1: Synthesis of glycerol-3-phosphate

- **Glycerol 3-phosphate is the initial acceptor of fatty acids during TAG synthesis.**
- **In both liver (the primary site of TAG synthesis) and adipose tissue, glucose → glycolysis  DHAP → glycerol 3-phosphate dehydrogenase → glycerol 3-phosphate.**
- **A second pathway found in the liver, but **not** in adipose tissue, uses **glycerol kinase** (adipose tissue are deficient in glycerol kinase)**

Step 1: Synthesis of glycerol-3-phosphate

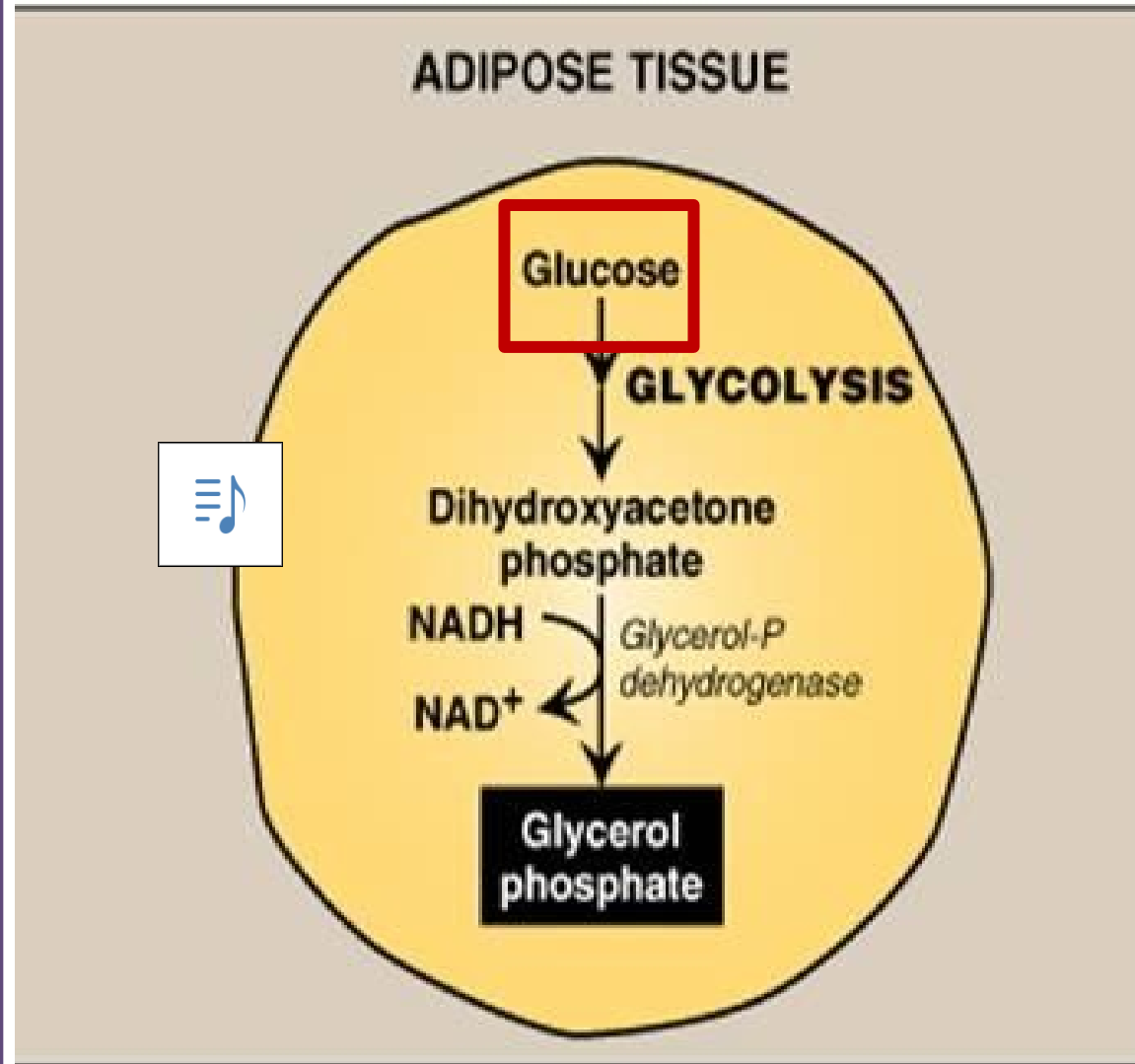


lippincott 6th edition p. 191

**present only in
liver not adipose
tissue**

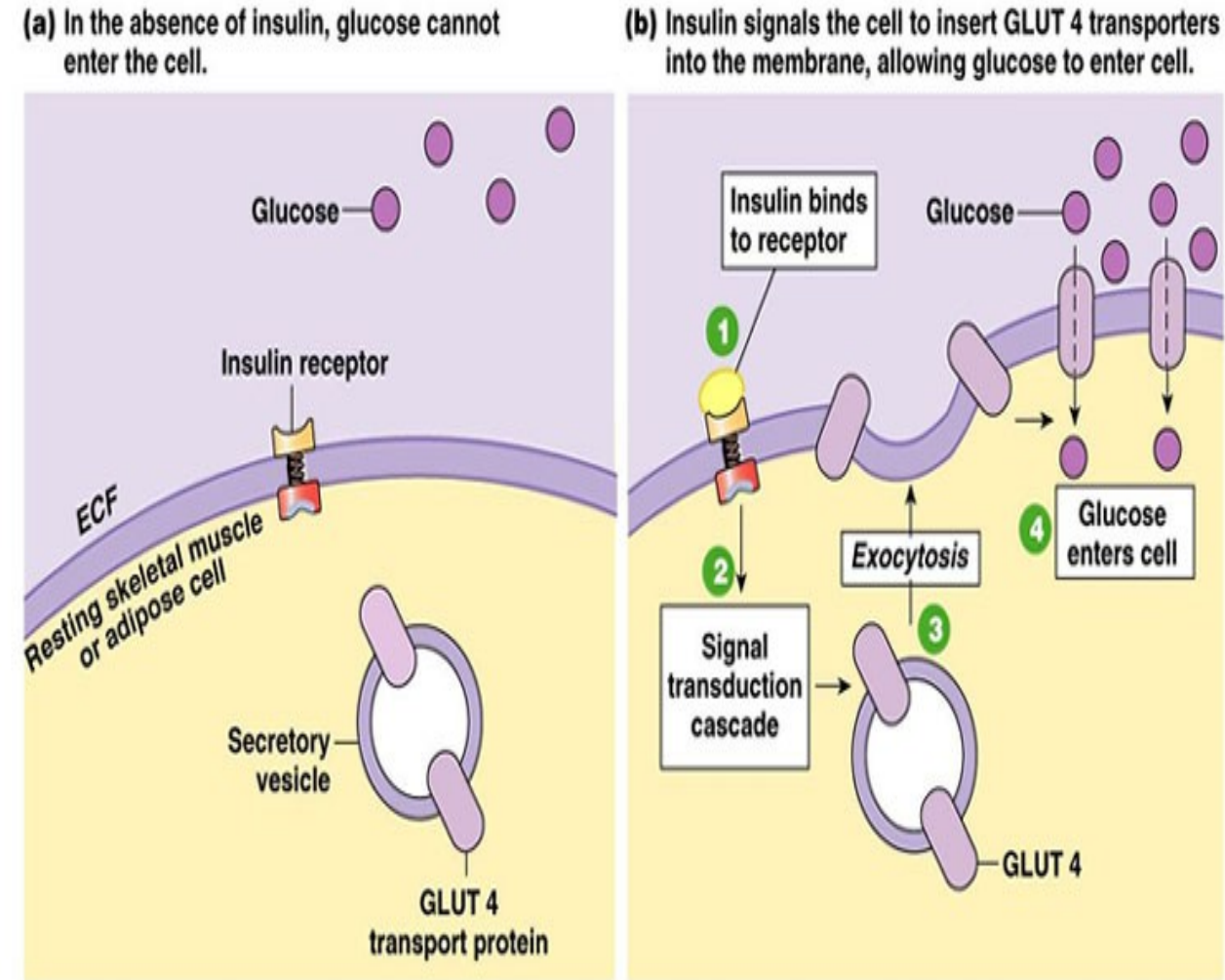
Step 1: Synthesis of glycerol-3-phosphate

DHAP only
in the
presence of
insulin.
So eating
excess
CHO causes
increased
body
weight.



Step 1: Synthesis of glycerol-3-phosphate

The glucose transporter in adipocytes (GLUT-4) is insulin dependent. Thus, when plasma glucose levels are low, adipocytes have only a limited ability to synthesize glycerol phosphate and cannot produce TAG de novo

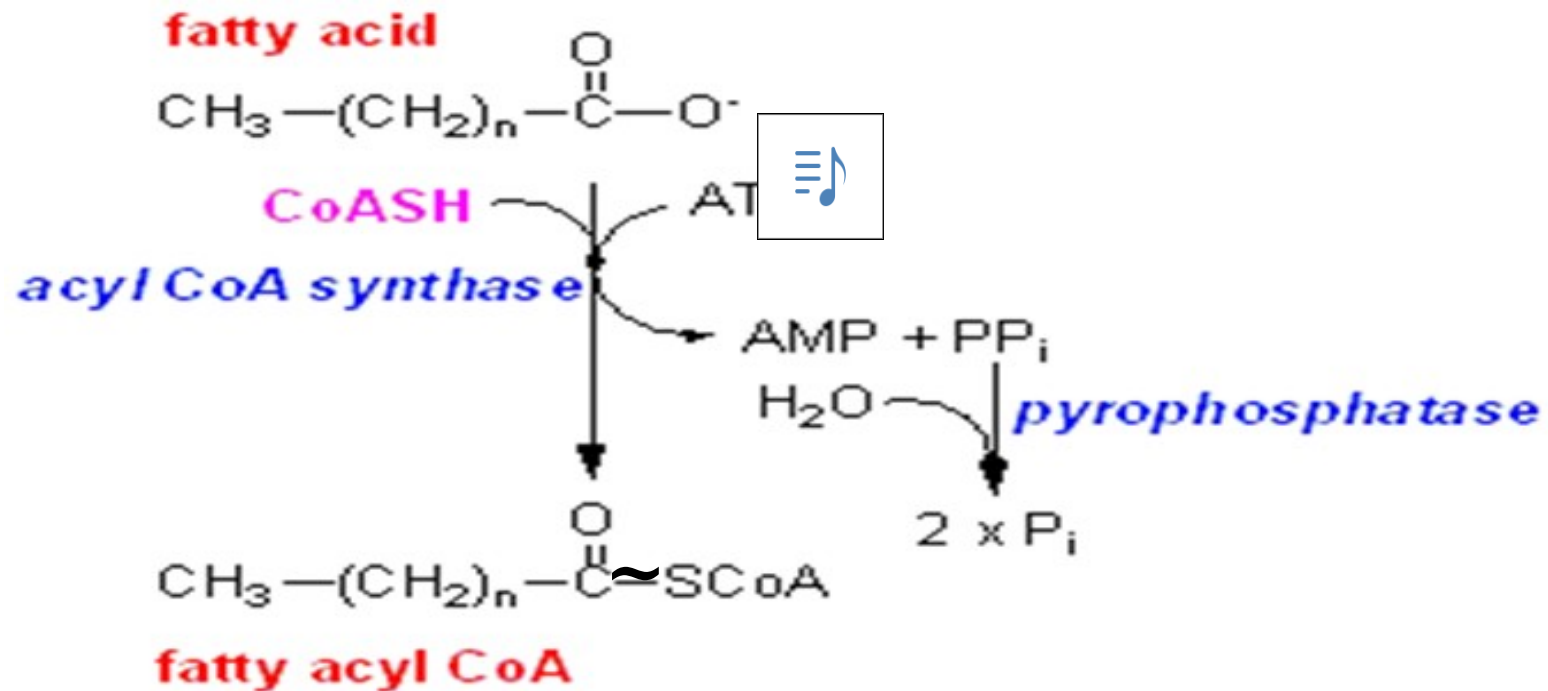


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Fig. 22-12

Step 2: Activation of the F.A

FAs are activated to form (acyl CoA) by Fatty acyl CoA synthetase (Thiokinase)



Step 3: Esterification

Glycerol

PO_4



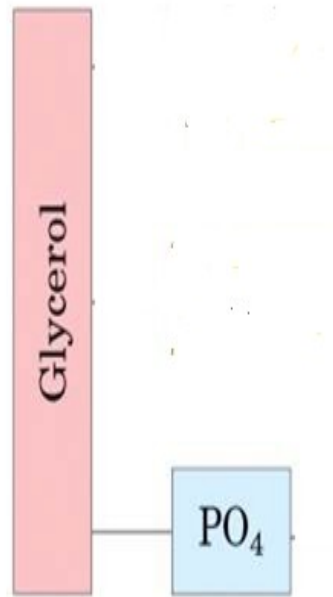
Glycerol

Fatty acid

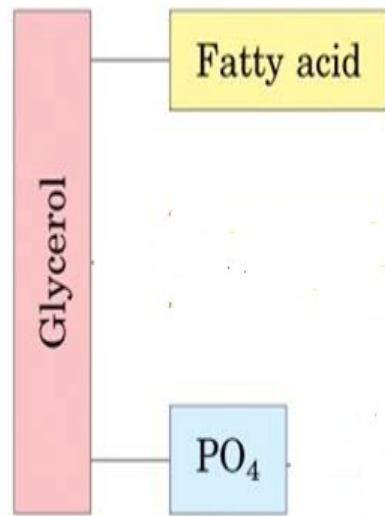
Fatty acid

Fatty acid

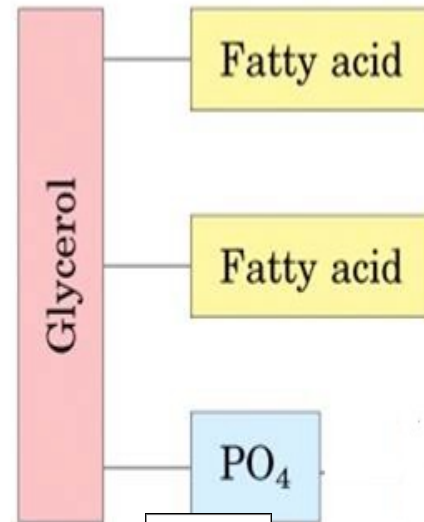




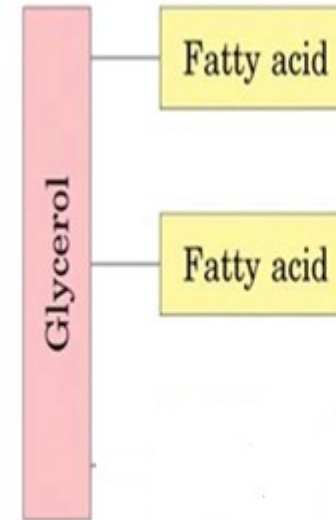
Glycerol-3-P



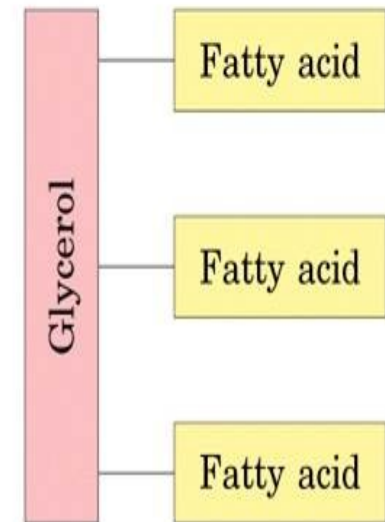
Lysophosphatidic acid



**Phosphatidic acid
(Diacylglycerolphosphate)**



DAG

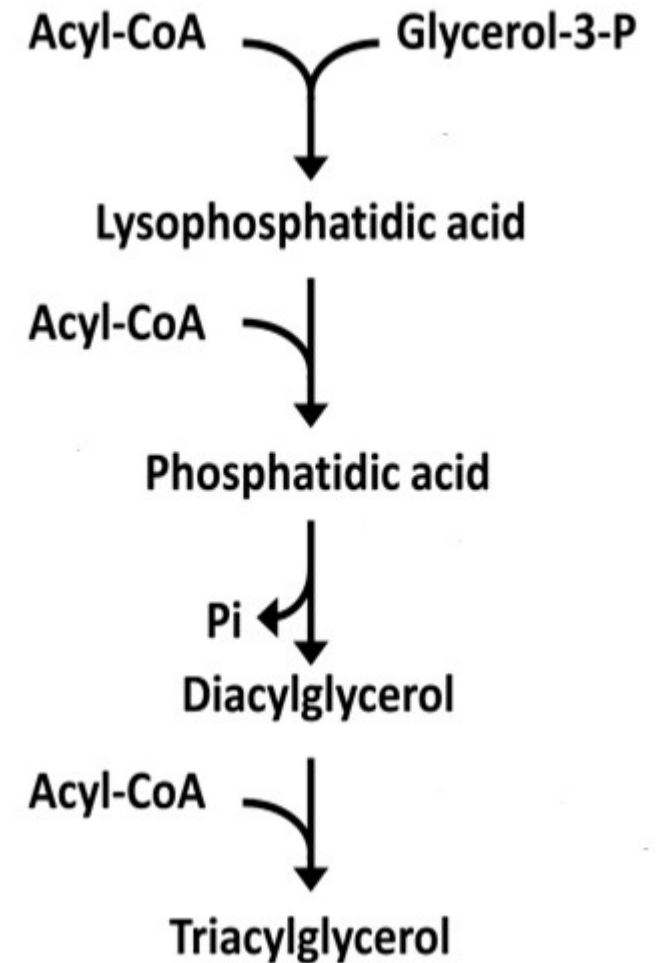


TAG

Step 3: Addition of 3 Acyl CoA to Glycerol-P (Esterification)

This pathway involves four reactions:

- the sequential addition of two fatty acids from fatty acyl CoAs,
- the removal of phosphate, and
- the addition of the third fatty acid.

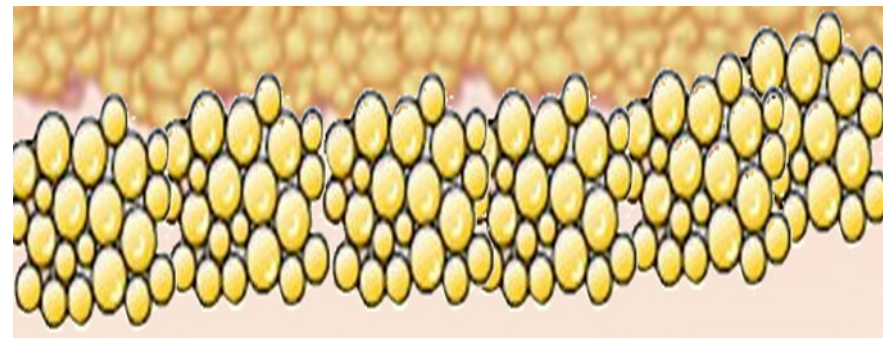


Edited from:
https://www.researchgate.net/figure/AGPAT-acyl-glycerol-3-phosphate-acyltransferase-CL-cardiolipin-DGK-diacylglycerol_fig1_51089275

Different Fates of TAG in Liver & Adipose Tissue

1- Adipose tissue

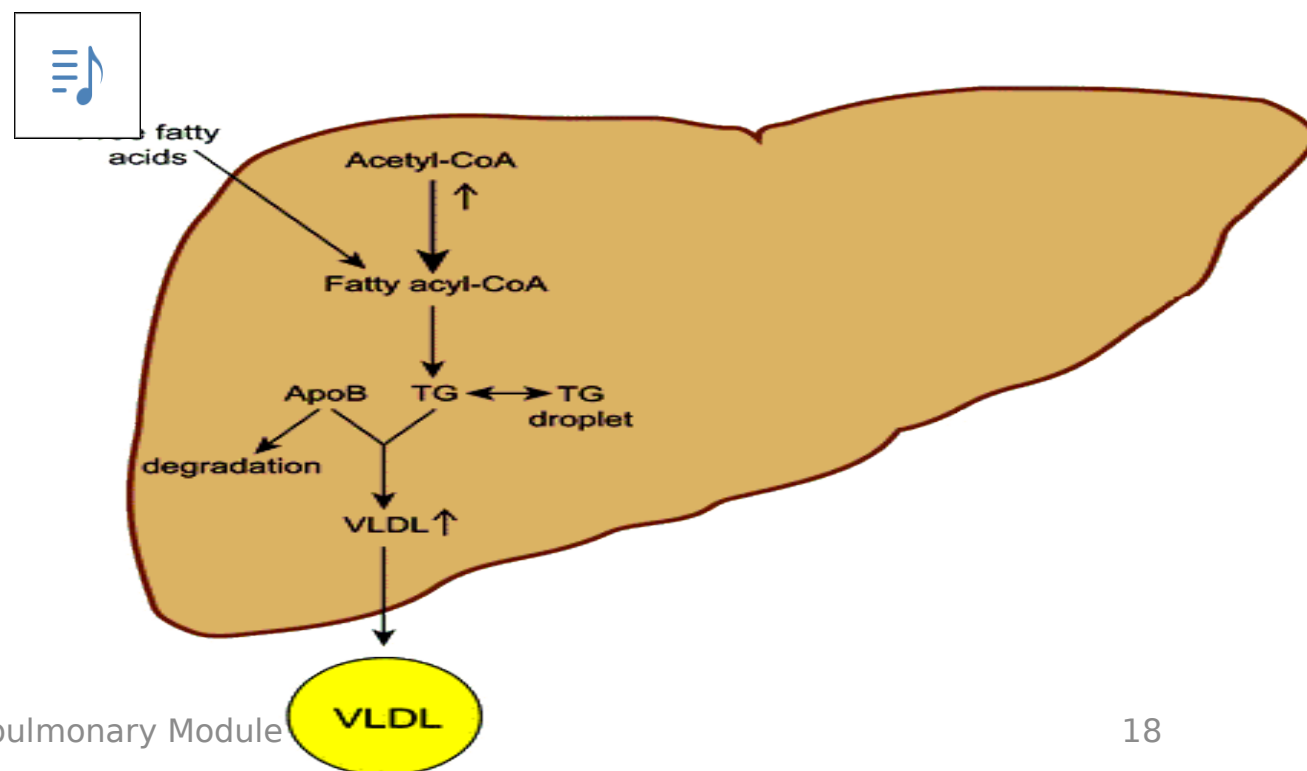
Stored in an anhydrous form ready for mobilization when the body requires it for fuel.



2- Liver

Little TAG is stored in liver.

Most of TAG is exported outside in the form of lipoproteins VLDL (Very Low Density Lipoproteins)



Adipose tissue lacks:

A- Hormone-sensitive lipase.

B- Glycerol kinase.

C- Glycerol-3-phosphate dehyd

D- Acetyl COA Carboxylase.

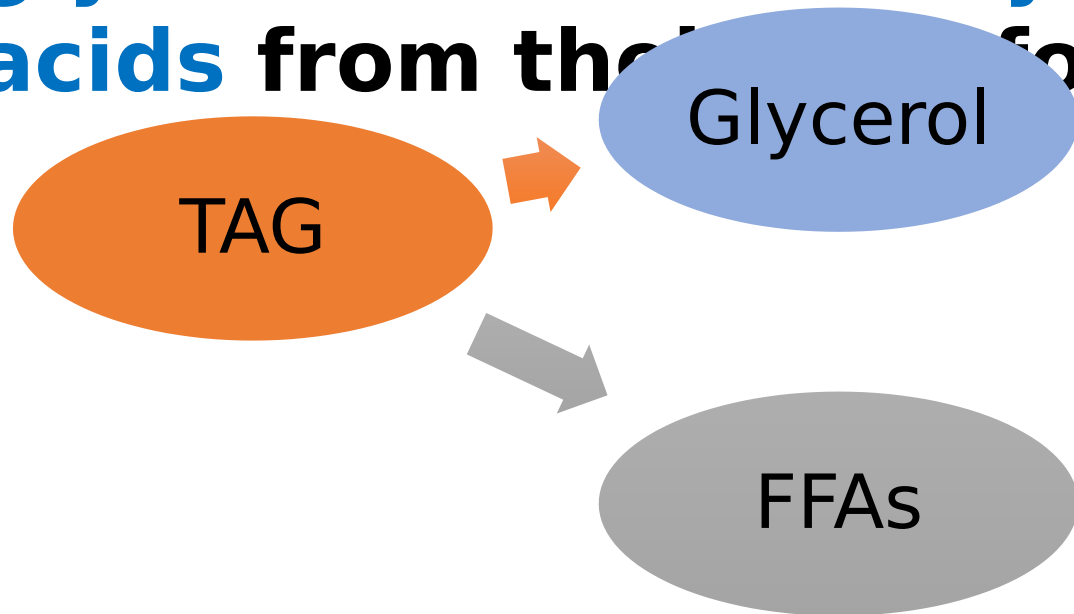


Lipolysis

(Mobilization of Stored Fat)

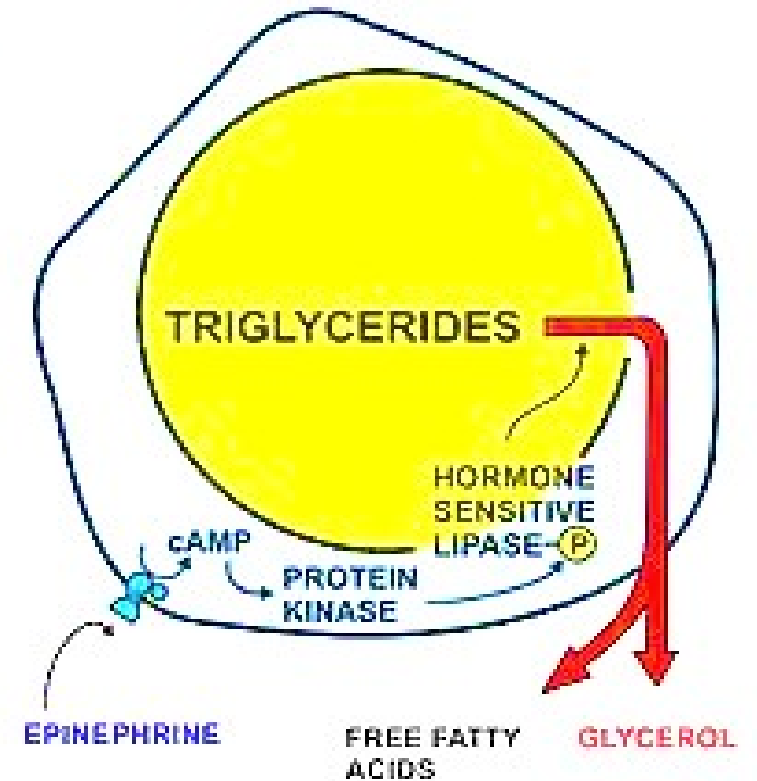


Definition: It is the hydrolytic release of **glycerol** and **free fatty acids** from the **triglycerides** for



LIPOLYSIS

IN THE ADIPOCYTE:



IN THE BLOOD:

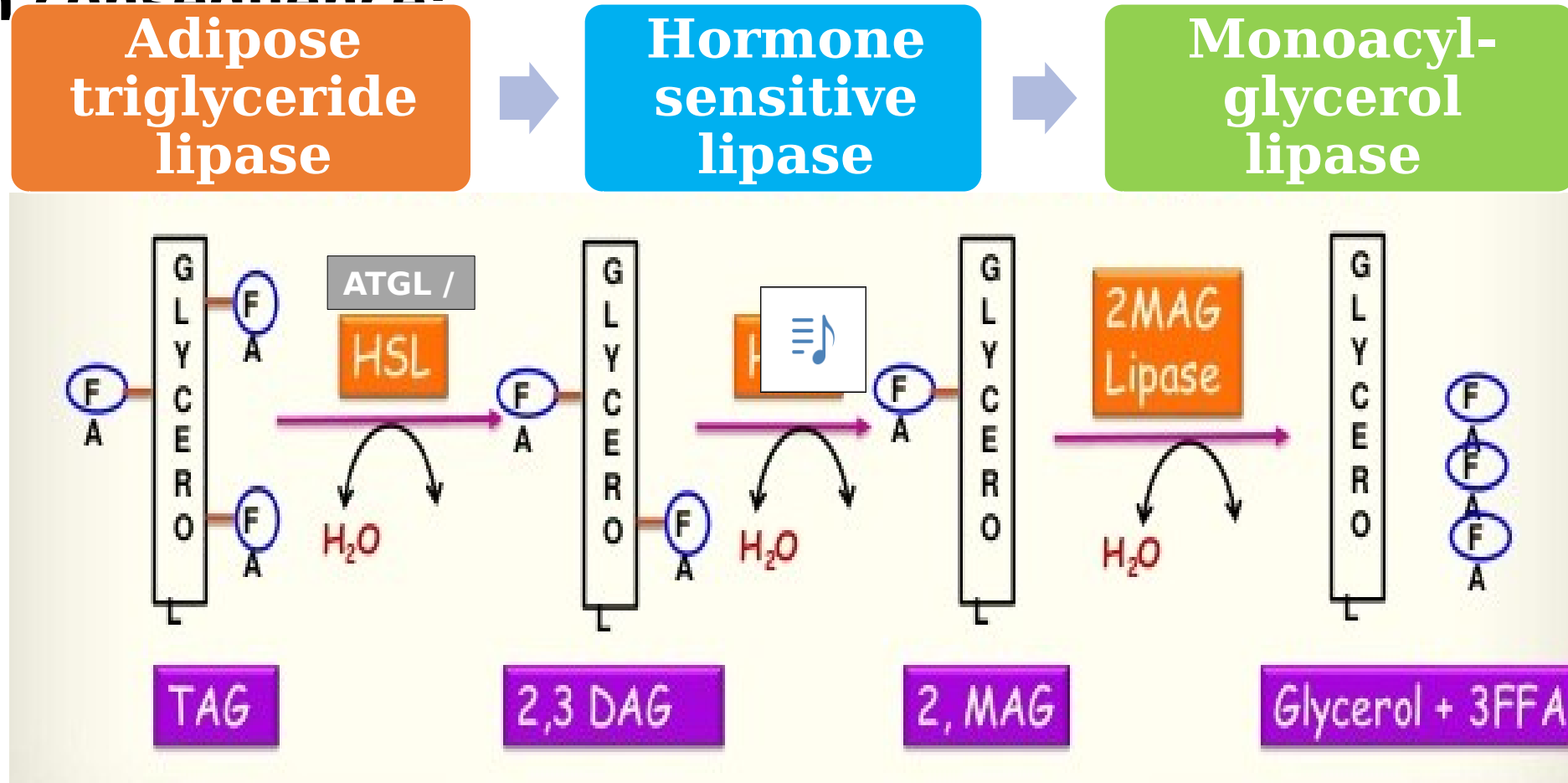
EPINEPHRINE

FREE FATTY
ACIDS

GLYCEROL

Lipolysis; Mechanism:

- Lipolysis is catalyzed by three Enzymes (lipases) working in consequence:



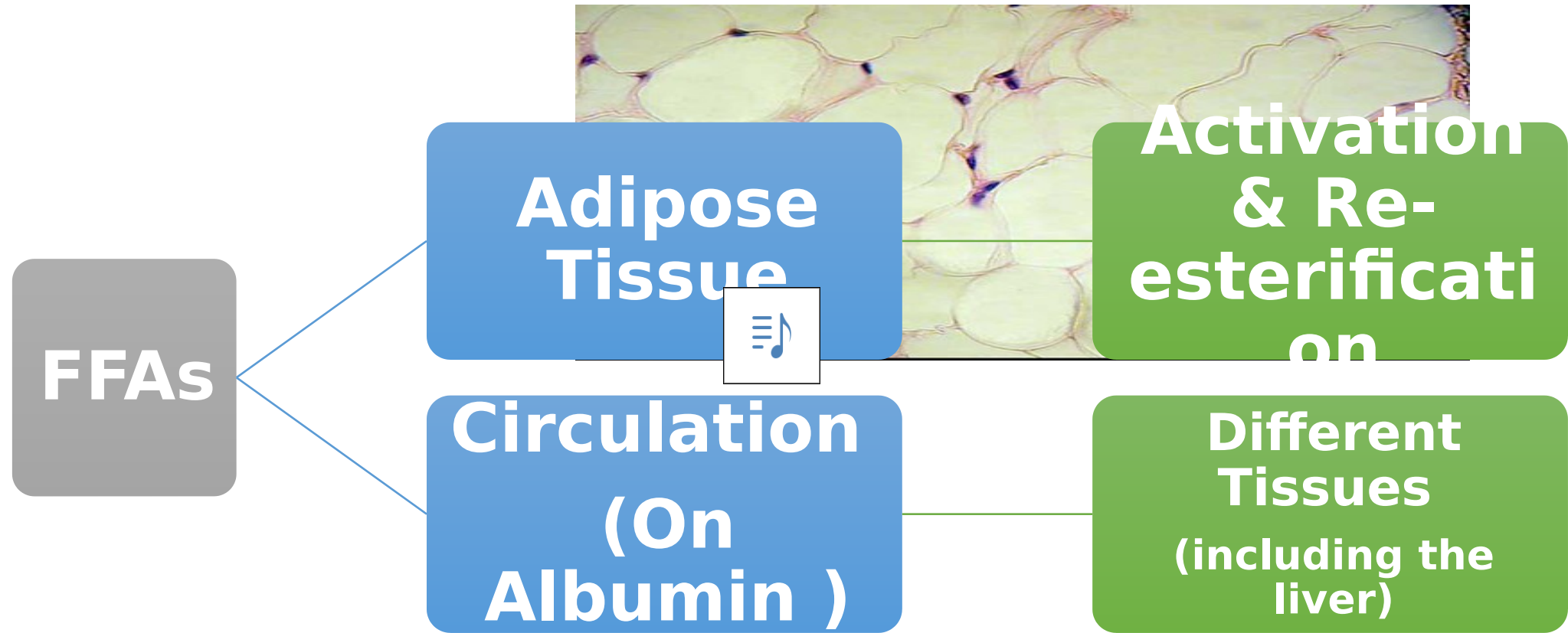
https://www.slideshare.net/ranajni_09/tag-metabolism

Lipolysis; Fate of Glycerol

It can not be metabolized by adipocytes due to **lack of glycerol kinase**, so it is transported through blood to liver to participate in **glycolysis** or **gluconeogenesis**.



Lipolysis; Fate of the FFAs:



The hydrolysis of adipose tissue triacylglycerol into glycerol and free fatty acids is called:

a. Fatty Acid oxidation

b. Esterification

c. lipolysis

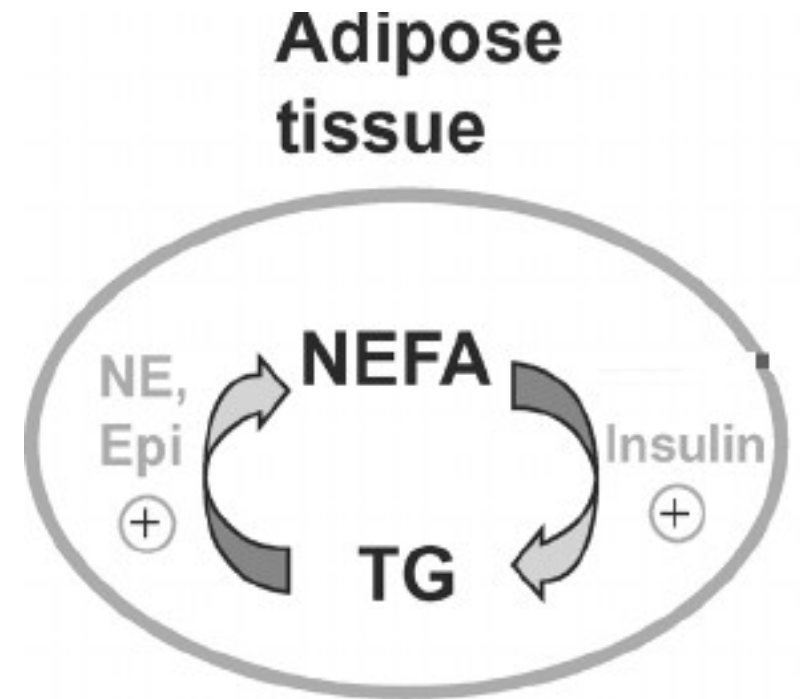
d. Lipogenesis

e. Glyceroneogenesis



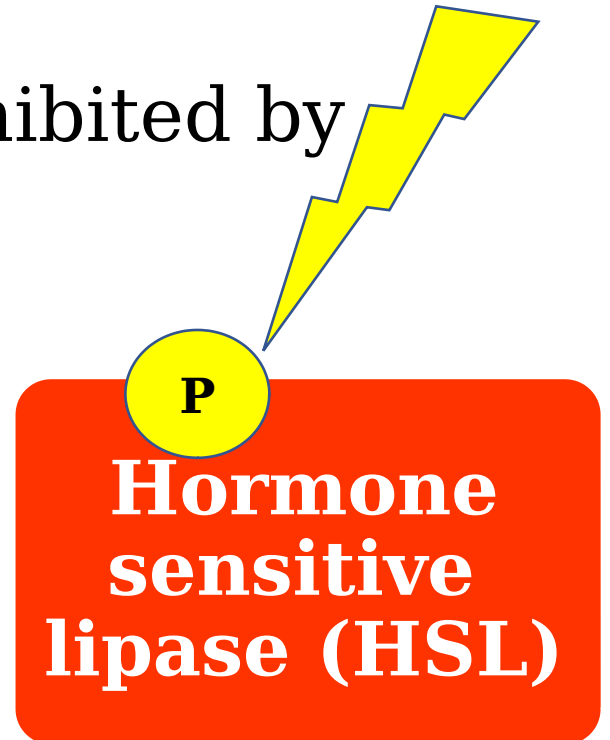
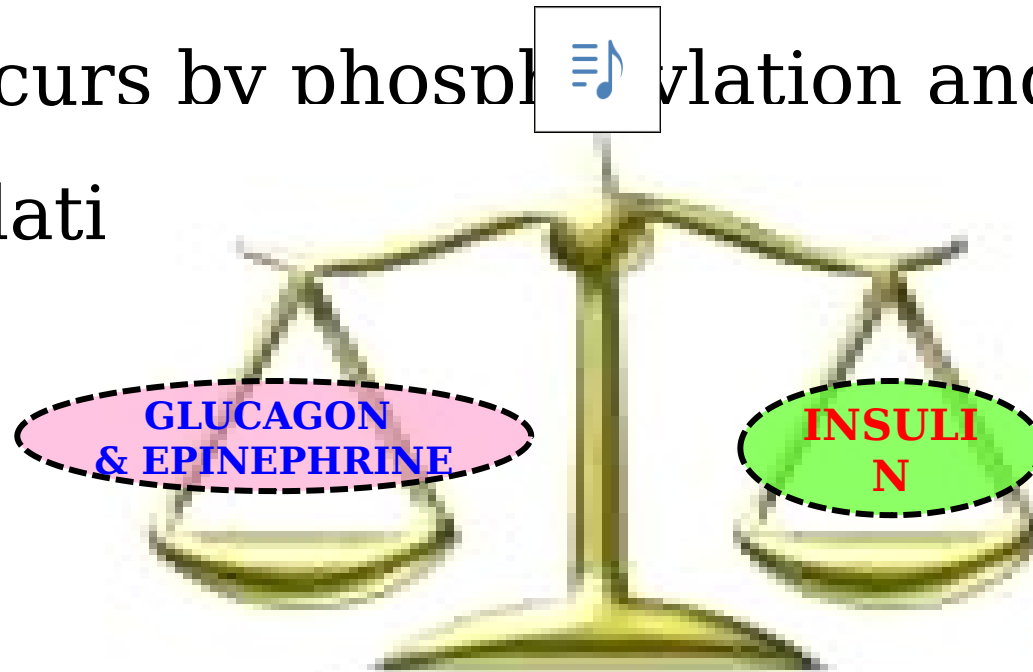
Regulation of Lipolysis

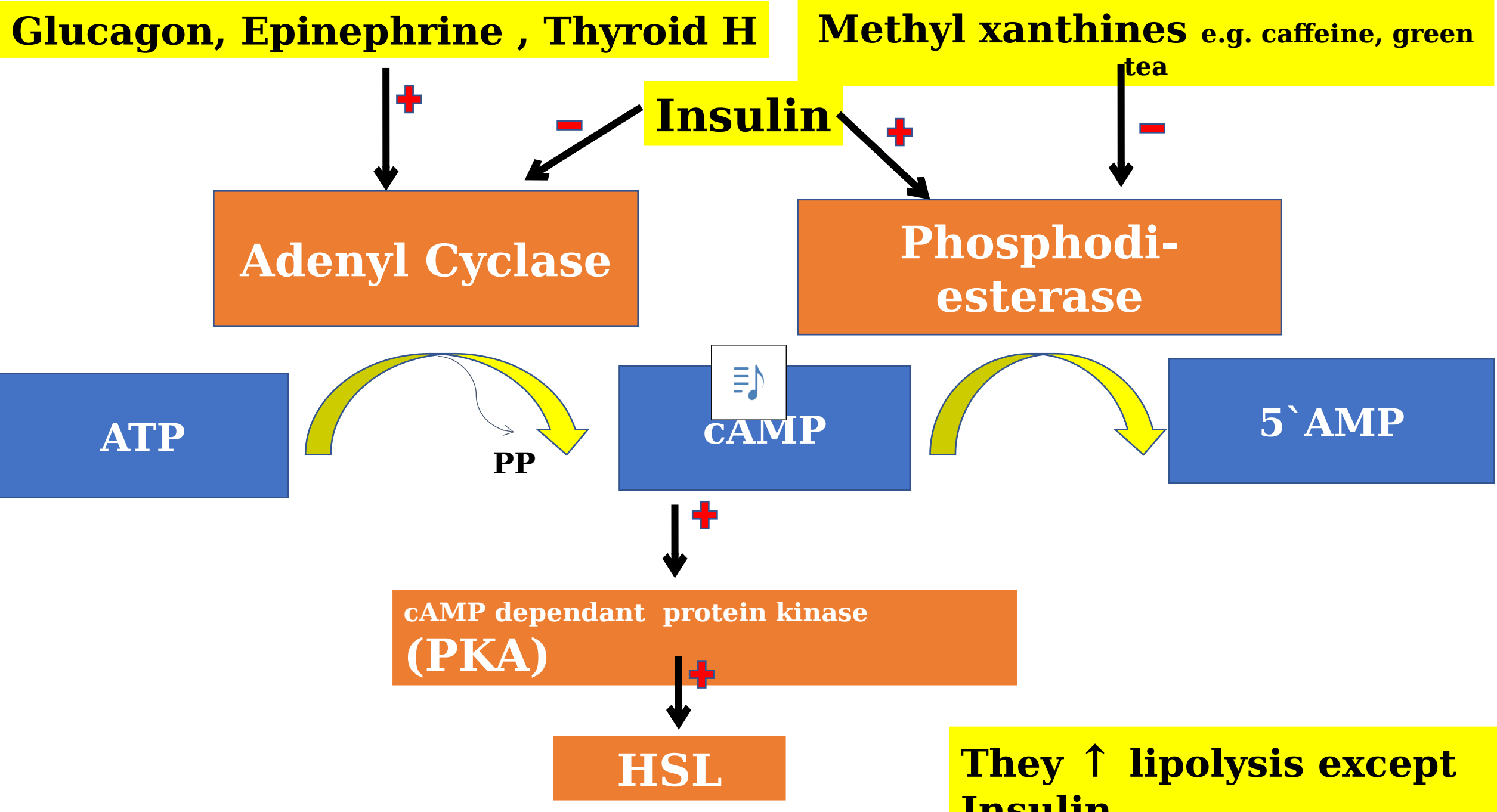
Triacylglycerol in adipose tissue is in dynamic state. It is continually formed and broken. The net of these two processes determines the amount of free fatty acids (FFA) released to the blood.



Regulation of Lipolysis

- HSL is the **key enzyme**. It is controlled by hormones.
- It has 2 forms; **phosphorylated** and **dephosphorylated**
- Activation occurs by phosphorylation and inhibited by dephosphorylation





Well fed state

Insulin



↑ cAMP phosphodiesterase, ↑ lipase phosphatase



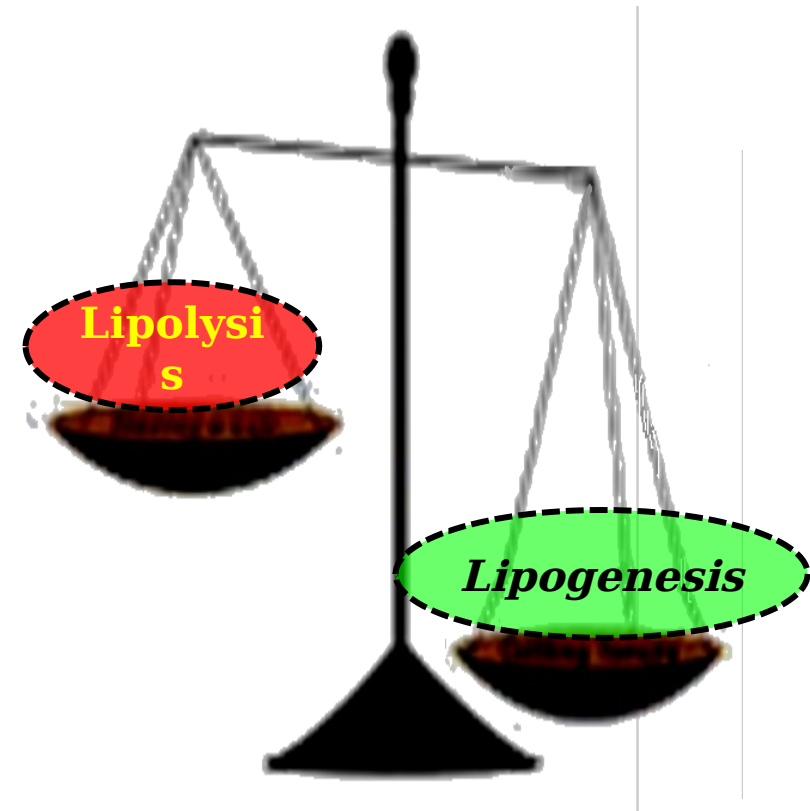
Dephosphorylation



Active ACC(acetyl COA carboxylase), ,
inactive HSL



(↑TAG synthesis, ↓ Degradation)



Fasting state

Glucagon, Epinephrin



↑ cAMP



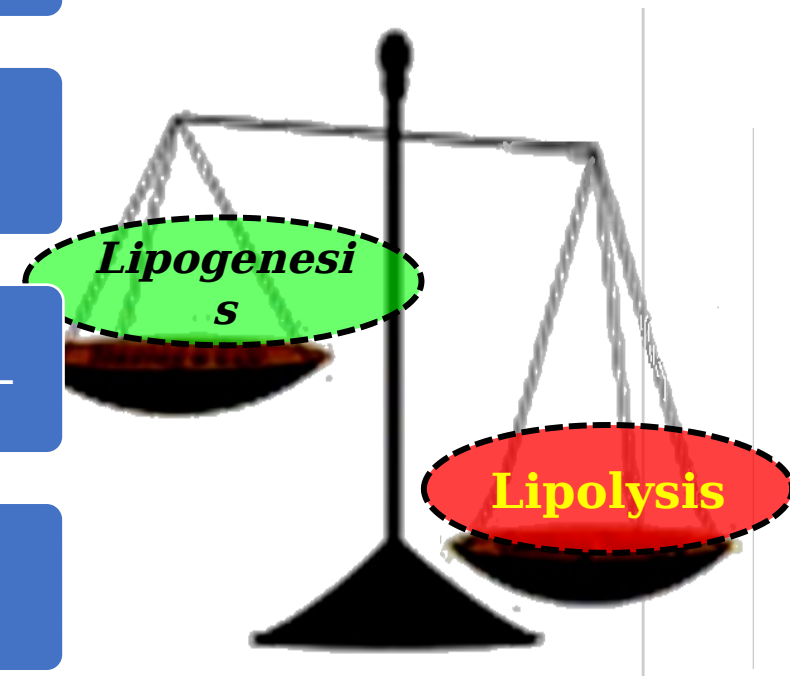
phosphorylation



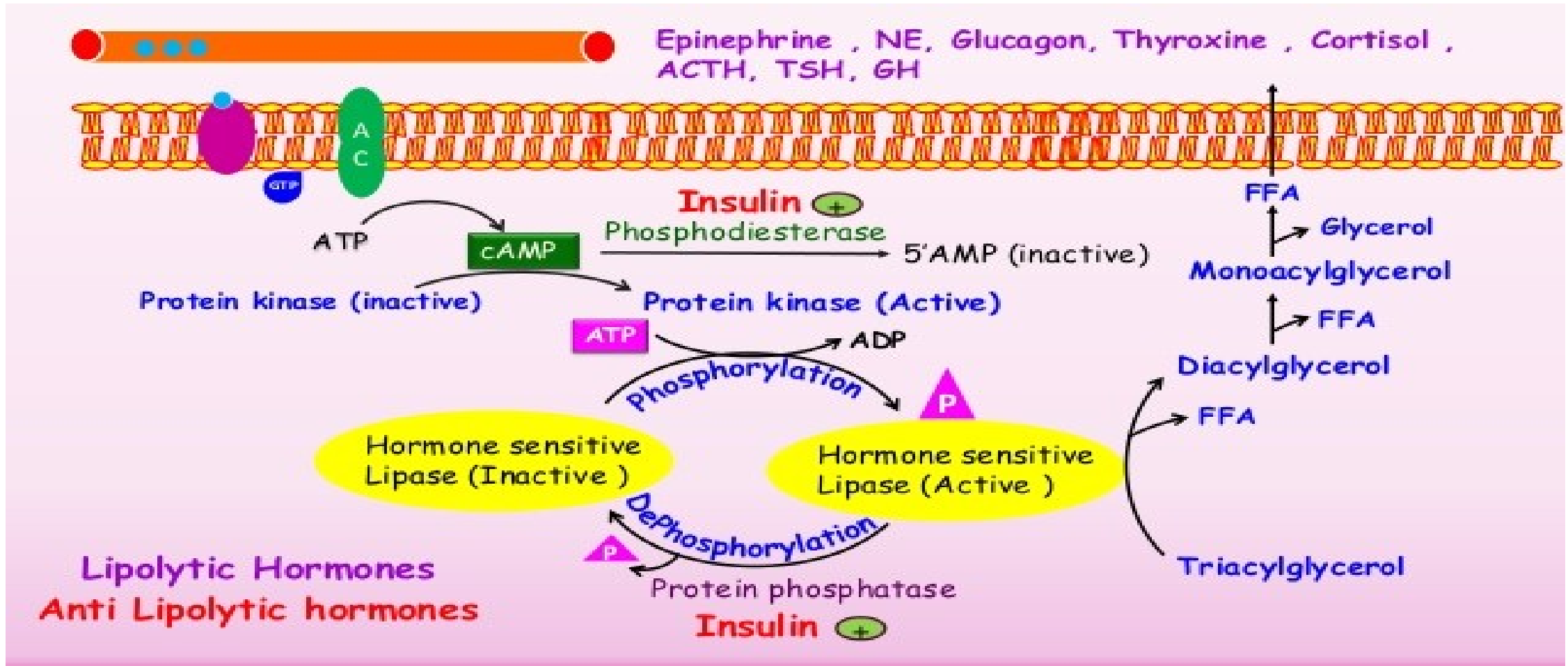
inactive ACC (acetyl COA carboxylase), Active HSL



↓ TAG synthesis, ↑ Degradation



Regulation of Lipolysis



https://www.slideshare.net/ranajni_09/tag-metabolism

Hepatic lipogenesis is stimulated by:

- a. AMP
- b. Epinephrine
- c. Glucagon
- ☒ d. Insulin
- e. Cortisol



Key Points:

- Liver is the primary site of TAG synthesis.
- In adipose tissue, glycerol-3-p comes mainly from glucose rather than glycerol.
- After synthesis, TAG has  different fates in liver & adipose tissue.
- The key enzyme of lipolysis is hormone sensitive lipase.
- Insulin decreases free fatty acids release from adipose tissue.

SUGGESTED TEXTBOOKS



1. "Lippincott's Illustrated Reviews in Biochemistry" by P.C.Champe, R.A.Harvey and D.R. Ferrier.
2. "Harper's Biochemistry" by R.K.Murray, D.K.Granner, P.A. Mayes and V.W. Rodwell.

Thank
you